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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/729,027

12/05/2003

Xin-Xing Gu

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EXAMINER

SHAHNAN SHAH, KHATOL S

ART UNIT

PAPER NUMBER

1645

DATE MAILED: 11/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/729,027

Applicant(s)

GU ET AL.

Examiner

Khatol S Shahnan-Shah

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 October 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-38 is/are pending in the application.
- 4a) Of the above claim(s) 1-20 and 35-38 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 21-34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-38 are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 05 December 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 12/05/2003.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

1. Applicants' Information Disclosure Statement, received December, 05, 2003 is acknowledged. Applicants listed 74 references that are of record in U.S. patent application No. 09/610,034 but did not submit copies of said references, however, the references from said application have been reviewed by the examiner. See attached PTO-1449.

Election/Restrictions

2. Applicants' election of October, 25 2004 without traverse is acknowledged. Applicants elected group III, claims 21-34 which are drawn to method of detoxifying a lipooligosaccharide and making a vaccine. Claims 1-20 and 35-38, are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions.

3. Currently claims 1-38 are pending.

4. Claims 21-34 are under consideration.

Priority

5. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78). Complete priority statement is missing from specification. The current status of the parent application (09/610,034) should be updated.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Note: Prior to establishing a prima facie case of obviousness the examiner wants to emphasize on the similarities and structure of lipooligosaccharides (LOS) and detoxified LOS (dLOS) in gram-negative bacteria and their role in production of immunogenic composition.

Major studies have been done on the LOS of *Neisseria meningitidis* (Gu et al., Infection and Immunity, Vol. 61, No. 5, pp. 1873-1880, May 1993), *Haemophilus influenzae* (Gu et al., Infection and Immunity, Vol. 63, No. 10, pp. 4115-4120, Oct, 1995; Gu et al., Infection and Immunity, Vol. 64, No. 10, pp. 4047-4053, Oct 1996; and Gu et al., Infection and immunity, Vol. 65, No. 11, pp. 4488-4493, Nov. 1997), *Vibrio cholera* (Gupta et al. Infection and Immunity, Vol. 60, No. 8, pp. 3201-3208, August, 1992) as potential vaccines. Also it is well known in the art that genera *Moraxella* (*Branhamella*), *Hemophilus* and *Neisseria* contain important human pathogens that can share ecological niches on mucosal surfaces. These non-enteric bacteria have outer membranes typical of gram-negative bacteria but their lipooligosaccharides lack O-antigenic side chain (Campagnari et al. Microbial Pathogenesis, Vol. 8, pp. 353-362, 1990). Campagnari et al. further teach that studies indicate that conservation of LOS exists among these organisms (see abstract and page 360). Edebrink et al. (Carbohydrate research Vol. 257, pp.269-284, 1994) teach structure of lipooligosaccharide isolated from *Moraxella catarrhalis*. Edebrink et al. teach that the lipopolysaccharide of *Moraxella catarrhalis* lacks O-antigenic side chains characteristic of enteric bacteria, thus being similar in general structure to the lipopolysaccharides of *Neisseria meningitidis*, *Neisseria gonorrhoeae*, *Haemophilus influenzae* and *Bordetella pertussis* (see page 270).

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8. Claims 21-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gu et al. (U.S. Patent Number 6,207,157) in view of Vaneechoutte et al. (Journal of Clinical Microbiology, Vol. 28, No.2, pp. 182-187, 1990.), Campagnari et al. (Microbial Pathogenesis, Vol. 8, pp. 353-362, 1990) and Edebrink et al. (Carbohydrate research Vol. 257, pp.269-284, 1994).

In the instant applications claims 21-22 are drawn to a method of detoxifying LOS and claims 23-34 are drawn to a method of making a conjugate vaccine.

Gu et al. teach a method of detoxifying a lipooligosaccharide comprising removing ester-linked fatty acids from LOS by treatment of LOS with hydrazine (see columns 3, 4, 7, 8 and claims).

Gu et al. teach a method of making a conjugate vaccine comprising removing ester-linked fatty acids from LOS to produce dLOS (see columns 3, 4, 7, 8 and claims). Gu et al. teach a LOS from which esterified fatty acids have been removed from lipid A to form a detoxified LOS (dLOS), and an immunogenic carrier (a protein) covalently linked thereto (see claims and columns 7-9). Gu et al. also teach linker compounds such as adipic acid dihydrazide, ϵ -aminohexanoic acid, chlorohexanol dimethyl acetal, D- glucuronolactone and p-nitrophenylethyl amine (see claims 5-7). Gu et al. do not teach lipooligosaccharide isolated from *Moraxella catarrhalis*. However, Vaneechoutte et al. teach immunogenic compositions comprising lipooligosaccharide isolated from *Moraxella (Barnhamella) catarrhalis* (see abstract and material and method page 182).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to detoxify the isolated lipooligosaccharides of Vaneechoutte et al. in view of teachings by Gu et al. to obtain the instant disclosure. Given the art-recognized fact that

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lipooligosaccharide epitopes shared among gram-negative non-enteric mucosal pathogens such as *Haemophilus influenzae* and *Moraxella catarrhalis* (Campagnari et al., see abstract, title and introduction) and the teaching of Edebrink et al. that the lipopolysaccharide of *Moraxella catarrhalis* lacks O-antigenic side chains characteristic of enteric bacteria, thus being similar in general structure to the lipopolysaccharides of, *Haemophilus influenzae* (see page 270) it would have been obvious to one having ordinary skill in the art to detoxify *Moraxella catarrhalis* lipopolysaccharide in view of teachings by Gu et al.

One having ordinary skill in the art would have been motivated by expectation of success and the attainment of a better methods and the fact that Gu et al. teach unexpected result that the dLOS conjugates obtained following detoxification are dramatically more effective than LOS (see figure 1) to apply the known method taught by Gu et al. to the isolated lipooligosaccharides from *Moraxella catarrhalis*.

Prior Citations of References

9. The references cited or used as prior art in support of one or more rejections in the instant office action have been previously cited and made of record in the parent application number 09/610,034 and applicants IDS. A PTO-892 has been submitted with this office action, however no copies of the references has been attached.

Conclusion

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol S Shahnan-Shah whose telephone number is (571)-272-0863. The examiner can normally be reached on 7:30am-4 pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F Smith can be reached on (571)-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).




Khatol Shahnan-Shah, BS, Pharm, MS

Biotechnology Patent Examiner

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November 13, 2004



RODNEY P SWARTZ, PH.D
PRIMARY EXAMINER